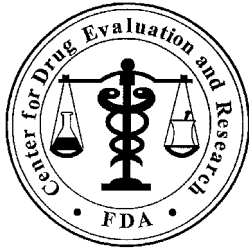


**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

***APPLICATION NUMBER:***

**22-411**

**PROPRIETARY NAME REVIEW(S)**



**Department of Health and Human Services**  
**Public Health Service**  
**Food and Drug Administration**  
**Center for Drug Evaluation and Research**  
**Office of Surveillance and Epidemiology**

Date: December 10, 2009

To: Thomas Laughren, MD, Director  
Division of Psychiatry Products

Through: Kellie Taylor, PharmD, MPH, Associate Director  
Carol Holquist, RPh, Director  
Division of Medication Error Prevention and Analysis (DMEPA)

From: Kate Gillette, PharmD Candidate, Pharmacy Intern  
Division of Medication Error Prevention and Analysis (DMEPA)

Subject: Proprietary Name Review

Drug Name(s): Oleptro (Trazodone HCl) Extended-release Tablet  
150 mg and 300 mg

Application Type/Number: NDA 22-411

Applicant: Labopharm

OSE RCM #: 2009-1549

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## **1 INTRODUCTION**

This re-assessment of the proposed proprietary name, Oleptro, is written in response to the anticipated approval of this NDA within 90 days from the date of this review. The Division of Medication Error Prevention and Analysis (DMEPA) found the proposed proprietary name, Oleptro, acceptable in OSE Review #2009-341, dated July 1, 2009. The Division of Psychiatry Drug Products did not have any concerns with the proposed name, Oleptro, and the Division of Drug Marketing, Advertising and Communication (DDMAC) found the name acceptable from a promotional perspective on February 13, 2009.

## **2 METHODS AND RESULTS**

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources (see section 4) to identify names with orthographic and/or phonetic similarity to the proposed name that have been approved since the previous proprietary name review. We used the same search criteria previously used in OSE Review #2009-341 and since none of the proposed product characteristics were altered we did not re-evaluate previous names of concern. Additionally, DMEPA searches the United States Adopted Names (USAN) stem list to determine if the name contains any USAN stems as of the last USAN updates. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proposed proprietary name, and focuses on the avoidance of medication errors.

The searches of the databases yielded one new name, Livalo, thought to look similar to Oleptro and represent a potential source of drug name confusion. This name was evaluated using FMEA. The findings of the FMEA indicate that the proposed name, Oleptro, is not likely to result in name confusion with Livalo for the reasons presented in Appendix A.

DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, Oleptro, as of December 7, 2009.

## **3 CONCLUSIONS AND RECOMMENDATIONS**

The proprietary name risk assessment findings indicate that the proposed name, Oleptro, is not vulnerable to name confusion that could lead to medication errors nor is the name considered promotional. Thus, the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Oleptro, for this product at this time.

DMEPA considers this a final review; however, if approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Psychiatry Drug Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new action date.

## 4 REFERENCES

1. OSE review # 2009-341, Proprietary Name Review of Oleptro, Kellie Taylor, Team Leader.

2. ***Drugs@FDA*** (<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>)

Drugs@FDA contains most of the drug products approved since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present.

Drugs@FDA contains official information about FDA approved [brand name](#), [generic drugs](#), [therapeutic biological products](#), [prescription](#) and [over-the-counter](#) human drugs and [discontinued drugs](#) and “[Chemical Type 6](#)” approvals.

3. ***USAN Stems*** (<http://www.ama-assn.org/ama/pub/category/4782.html>)

USAN Stems List contains all the recognized USAN stems.

4. ***CDER Proposed Names List***

Compiled list of proposed proprietary names submitted to the Division of Medication Error Prevention and Analysis (DMEPA) for review. The list is updated weekly and maintained by DMEPA.

**Appendix A: Product with no overlap in strength or dose**

<b>Product name with potential for confusion</b>	<b>Similarity to Proposed Proprietary Name</b>	<b>Strength</b>	<b>Usual Dose (if applicable)</b>
<b>Oleptro</b>	<b>N/A</b>	<b>150 mg, 300 mg</b>	<b>150 to 375 mg every evening</b>
Livalo (pitavastatin)	Orthographic	1 mg, 2 mg, 4 mg	1 to 4 mg once daily

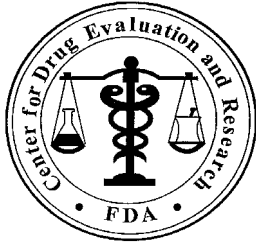
Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22411	ORIG-1	LABOPHARM INC	TRAZODONE CONTRAMID OAD E-R CAPLET

**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**

/s/

KELLIE A TAYLOR  
01/06/2010

CAROL A HOLQUIST  
01/06/2010



**Department of Health and Human Services  
Public Health Service  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Surveillance and Epidemiology**

Date: July 1, 2009

To: Thomas Laughren, MD, Director  
Division of Psychiatry Products

Through: Carol Holquist, RPh, Director  
Division of Medication Error Prevention and Analysis

From: Kellie Taylor, PharmD, MPH, Team Leader  
Division of Medication Error Prevention and Analysis

Subject: Proprietary Name Review

Drug Name(s): Oleptro (Trazodone HCl) Extended-release Tablets  
150 mg and 300 mg

Application Type/Number: NDA 22-411

Applicant/sponsor: Labopharm

OSE RCM #: 2009-341



## EXECUTIVE SUMMARY

The re-assessment of this proprietary name is written in response to a notification that a regulatory action on NDA 22-411 will occur within 90 days. DMEPA found the proposed proprietary name, Oleptro, acceptable in OSE Review #2008-1551 on February 13, 2009. Since that review, none of Oleptro's product characteristics have changed.

During this re-review we identified six new names for their similarity to Oleptro. The results of the Failure Mode Effects Analysis found that the proposed name, Oleptro, is not vulnerable to name confusion that could lead to medication errors with any of six names. Thus, the Division of Medication Error Prevention and Analysis finds the proprietary name, Oleptro, acceptable for this product.

DMEPA considers this a final review, however, if approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Psychiatry Products should notify DMEPA because the proprietary name must be re-reviewed prior to the anticipated action date.

## 1 METHODS AND MATERIALS

Appendix A describes the general methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a re-assessment of a proprietary name 90 days prior to approval of an application. Section 1.1 identifies the specific search criteria associated with the proposed proprietary name, Oleptro.

### 1.1 PROPRIETARY NAME RISK ASSESSMENT

For this review, particular consideration was given to drug names beginning with the letter 'O' when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.<sup>12</sup>

To identify drug names that may look similar to Oleptro, the staff also consider the other orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (seven letters), upstrokes (three, capital letter 'O', 'I', and 't'), downstrokes (one, if "p" is scripted), cross-strokes (one, 't'), and dotted letters (none). Additionally, several letters in Oleptro may be vulnerable to ambiguity when scripted, including the letter 'O' may appear as 'A' or 'U'; lower case 'o' appear as a lower case 'a' or 'u'. As such, the staff should also consider these alternate appearances when identifying drug names that may look similar to Oleptro.

When searching to identify potential names that may sound similar to Oleptro, the medication error staff search for names with similar number of syllables (three), stresses (O- lep-tro or o-LEP-tro or o-lep-TRO), consonant sound pronunciation ("O versus "UH" or '-lep-' versus '-leap-'), and placement of vowel and consonant sounds. In addition, several letters in Oleptro may be subject to misinterpretation when spoken, including the letter 'O' which may be interpreted as 'U' and the letter 'e' may be misinterpreted as 'i'. As such, the staff also considers these alternate pronunciations when identifying drug names that may sound similar to Oleptro. The Applicant's intended pronunciation of the proprietary

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<sup>1</sup> Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at <http://www.ismp.org/Tools/confuseddrugnames.pdf>

<sup>2</sup> Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artificial Intelligence in Medicine (2005)

name could not be expressly taken into consideration, as this was not provided with the proposed name submission.

## **2 RESULTS**

### **2.1 DATABASE AND INFORMATION SOURCES**

The searches of the databases listed in Section 5.2 yielded a total of seven names as having some similarity to the name Oleptro.

Five of the seven names were thought to look like Oleptro, which include: Acular, Atripla, Oforta\*\*\*, Olestra, and Arixtra. Two names, Oleptal and (b) (4), were thought to sound similar to Oleptro.

A search of the United States Adopted Names (USAN) stem list on June 29, 2009 identified no USAN stems contained in the proposed name, Oleptro.

### **2.2. EXPERT PANEL DISCUSSION**

The Expert Panel reviewed the pool of names identified by the DMEPA staff (see section 2.1 above), and noted no additional names thought to have orthographic or phonetic similarity to Oleptro.

DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name.

### **2.3 SAFETY EVALUATOR RISK ASSESSMENT**

Independent searches by the primary Safety Evaluator did not identify any additional names thought to look similar to Oleptro and represent a potential source of drug name confusion.

Olestra was identified in the previous Oleptro proprietary name review (OSE Review 2008-1551, dated February 13, 2009). None of Oleptro's product characteristics have changed since the previous review. Therefore, the original assessment is maintained. Please see the previous review for a detailed analysis of this name.

## **3 DISCUSSION**

DDMAC had no concerns with the proposed name, Oleptro, from a promotional perspective.

We identified and evaluated six names for their potential similarity to the proposed name, Oleptro. Four names lacked orthographic and/or phonetic similarity to Oleptro and were not evaluated further (See Appendix B).

Failure mode and effect analysis (FMEA) was then applied to determine if the proposed name could potentially be confused with the remaining two names and lead to medication errors. This analysis determined that the name similarity between Oleptro was unlikely to result in medication errors with the two products for the reasons presented in Appendices C and D.

## **4 CONCLUSIONS AND RECOMMENDATIONS**

The Proprietary Name Risk Assessment findings indicate that the proposed name, Oleptro, is not vulnerable to name confusion that could lead to medication errors. As such, we do not object to the use of the proprietary name, Oleptro, for this product.

DMEPA considers this a final review; however, if approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Psychiatry Products should notify DMEPA because the proprietary name must be re-reviewed prior to the anticipated action date.

## **5 REFERENCES**

### **5.1 OSE REVIEWS**

Lee, JJ. OSE Review 2008-1551: Proprietary Name Review for Oleptro. 13 February 2009.

### **5.2 DATABASES**

#### **1. *Micromedex Integrated Index* (<http://weblern/>)**

Contains a variety of databases covering pharmacology, therapeutics, toxicology and diagnostics.

#### **2. *Phonetic and Orthographic Computer Analysis (POCA)***

As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists which operates in a similar fashion. This is a database which was created for the Medication Error Prevention Staff, FDA.

#### **3. *Drug Facts and Comparisons, online version, St. Louis, MO* (<http://weblern/>)**

Drug Facts and Comparisons is a compendium organized by therapeutic Course; contains monographs on prescription and OTC drugs, with charts comparing similar products.

#### **4. *AMF Decision Support System [DSS]***

DSS is a government database used to track individual submissions and assignments in review divisions.

#### **5. *Division of Medication Error Prevention proprietary name consultation requests***

This is a list of proposed and pending names that is generated by the Medication Error Prevention Staff from the Access database/tracking system.

#### **6. *Drugs@FDA* (<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>)**

Drugs@FDA contains most of the drug products approved since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA approved [brand name](#) and [generic drugs](#) and [therapeutic biological products](#); [prescription](#) and [over-the-counter](#) human drugs and [therapeutic biologicals](#), [discontinued drugs](#) and “[Chemical Type 6](#)” approvals.

#### **7. *Electronic online version of the FDA Orange Book* (<http://www.fda.gov/cder/ob/default.htm>)**

Provides a compilation of approved drug products with therapeutic equivalence evaluations.

**8. US Patent and Trademark Office location** <http://www.uspto.gov>.

Provides information regarding patent and trademarks.

**9. Clinical Pharmacology Online** (<http://weblern/>)

Contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. Provides a keyword search engine.

**10. Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at** [www.thomson-thomson.com](http://www.thomson-thomson.com)

The Pharma In-Use Search database contains over 400,000 unique pharmaceutical trademarks and tradenames that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

**11. Natural Medicines Comprehensive Databases** (<http://weblern/>)

Contains up-to-date clinical data on the natural medicines, herbal medicines, and dietary supplements used in the western world.

**12. Stat!Ref** (<http://weblern/>)

Contains full-text information from approximately 30 texts. Includes tables and references. Among the database titles are: Handbook of Adverse Drug Interactions, Rudolphs Pediatrics, Basic Clinical Pharmacology and Dictionary of Medical Acronyms Abbreviations.

**13. USAN Stems** (<http://www.ama-assn.org/ama/pub/category/4782.html>)

List contains all the recognized USAN stems.

**14. Red Book Pharmacy's Fundamental Reference**

Contains prices and product information for prescription, over-the-counter drugs, medical devices, and accessories.

**15. Lexi-Comp** ([www.pharmacist.com](http://www.pharmacist.com))

A web-based searchable version of the Drug Information Handbook.

**16. Medical Abbreviations Book**

Contains commonly used medical abbreviations and their definitions.

## APPENDICES

### **Appendix A:**

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, BLA, and ANDA products currently under review by the Center. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.<sup>3</sup>

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity and hold a Center for Drug Evaluation and Research (CDER) Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name.

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and focuses on the avoidance of medication errors.

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail.<sup>4</sup> DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product.

In addition, the product characteristics provide the context for the verbal and written communication of the drug names and can interact with the orthographic and phonetic attributes of the names to increase the risk of confusion when there is overlap or, in some instances, decrease the risk of confusion by helping to differentiate the products through dissimilarity. Accordingly, the DMEPA staff considers the product characteristics associated with the proposed drug throughout the risk assessment because the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, DMEPA staff considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and

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<sup>3</sup> National Coordinating Council for Medication Error Reporting and Prevention.  
<http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.

<sup>4</sup> Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

monitoring the impact of the medication.<sup>5</sup> DMEPA provides the product characteristics considered for this review in section one.

The Division of Medication Error Prevention and Analysis considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compares the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. DMEPA staff also examines the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly and even dissimilarly spelled drug name pairs to appear very similar to one another. The similar appearance of drug names when scripted has led to medication errors. The DMEPA staff applies expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g., “T” may look like “F,” lower case ‘a’ looks like a lower case ‘u,’ etc). Additionally, other orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details). In addition, the DMEPA staff compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. If provided, DMEPA will consider the Applicant’s intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Applicant has little control over how the name will be spoken in clinical practice.

**Table 1.** Criteria used to identify drug names that look- or sound-similar to a proposed proprietary name.

<b>Type of similarity</b>	<b>Considerations when searching the databases</b>		
	<i>Potential causes of drug name similarity</i>	<i>Attributes examined to identify similar drug names</i>	<i>Potential Effects</i>
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	<ul style="list-style-type: none"> <li>Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication</li> <li>Names may look similar when scripted and lead to drug name confusion in written communication</li> </ul>
	Orthographic similarity	Similar spelling Length of the name Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	<ul style="list-style-type: none"> <li>Names may look similar when scripted, and lead to drug name confusion in written communication</li> </ul>

<sup>5</sup> Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	<ul style="list-style-type: none"> <li>Names may sound similar when pronounced and lead to drug name confusion in verbal communication</li> </ul>
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Lastly, the DMEPA staff also considers the potential for the proposed proprietary name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. Consequently, DMEPA considers and evaluates these broader safety implications of the name throughout this assessment and the medication error staff provides additional comments related to the safety of the proposed proprietary name or product based on professional experience with medication errors.

### 1. Database and Information Sources

DMEPA staff conducts searches of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name using the criteria outlined in Section 2.1. Section 6 provides a standard description of the databases used in the searches. To complement the process, the DMEPA staff use a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the DMEPA staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel.

### 2. CDER Expert Panel Discussion

DMEPA conducts an Expert Panel Discussion to gather CDER professional opinions on the safety of the proposed product and the proposed proprietary name. The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

The primary Safety Evaluator presents the pooled results of the DMEPA staff to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend the addition of names, additional searches by the primary Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

### 3. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, conducts a Failure Mode and Effects Analysis, and provides an overall risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a

systematic tool for evaluating a process and identifying where and how it might fail.<sup>6</sup> When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Section one. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name to all of the names gathered from the above searches, Expert Panel Discussion, and prescription studies, external studies, and identifies potential failure modes by asking:

***“Is the proposed proprietary name convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting?”***

An affirmative answer indicates a failure mode and represents a potential for the proposed proprietary name to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names possess similarity that would cause confusion at any point in the medication use system, thus the name is eliminated from further review.

In the second stage of the Risk Assessment, the primary Safety Evaluator evaluates all potential failure modes to determine the likely *effect* of the drug name confusion, by asking:

***“Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?”***

The answer to this question is a central component of the Safety Evaluator’s overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would not ultimately be a source of medication errors in the usual practice setting, the primary Safety Evaluator eliminates the name from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend the use of an alternate proprietary name.

DMEPA will object to the use of proposed proprietary name when the primary Safety Evaluator identifies one or more of the following conditions in the Risk Assessment:

1. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with DDMAC’s findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].

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<sup>6</sup> Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.



2. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].
3. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
4. The proposed proprietary name contains an USAN (United States Adopted Names) stem.
5. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the Applicant select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the Applicant with recommendations that reduce or eliminate the potential for error and, thereby, would render the proposed name acceptable.

In the event that DMEPA objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, DMEPA will provide a contingency objection based on the date of approval. Whichever product, the Agency approves first has the right to use the proprietary name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

The threshold set for objection to the proposed proprietary name may seem low to the Applicant. However, the safety concerns set forth in criteria a through e are supported either by FDA regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), Joint Commission on Accreditation of Hospitals (JCOAH), and the Institute for Safe Medication Practices (ISMP). These organizations have examined medication errors resulting from look- or sound-alike drug names and called for regulatory authorities to address the issue prior to approval. Additionally, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and a preventable source of medication error that, in many instances, the Agency and/or Applicant can identify and rectify prior to approval to avoid patient harm.

Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Applicants have undertaken higher-leverage strategies, such as drug name changes, in the past but at great financial cost to the Applicant and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Applicants' have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval.

**Appendix B:** Proprietary names with minimal orthographic and/or phonetic similarity

Proprietary Name
Acular
Oforta***
Arixtra
(b) (4)

**Appendix C:** Proprietary names used only in foreign countries

Proprietary Name	Similarity to Oleptro	Country
Oleptal (oxcarbazepine 150mg, 300mg, 600 mg)	Look	Brazil

**Appendix E:** Products with no overlap in strength or dose

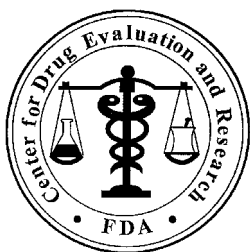
Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength
Oleptro (Trazoldone HCl) extended-release tablets		150 mg, 300mg
Atripla (Efavirenz, emtricitabine, and tenofovir disoproxil fumarate)	Look	600mg/200mg/300mg

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/s/

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Kellie Taylor  
7/1/2009 10:37:34 AM  
DRUG SAFETY OFFICE REVIEWER

Carol Holquist  
7/2/2009 08:55:25 AM  
DRUG SAFETY OFFICE REVIEWER



**Department of Health and Human Services**  
**Public Health Service**  
**Food and Drug Administration**  
**Center for Drug Evaluation and Research**  
**Office of Surveillance and Epidemiology**

Date: February 13, 2009

To: Thomas Laughren, MD, Director  
Division of Psychiatry Products

Thru: Kellie Taylor, PharmD, MPH, Team Leader  
Denise Toyer, PharmD, Deputy Director  
Carol Holquist, RPh, Director  
Division of Medication Error Prevention and Analysis

From: Jinhee J. Lee, PharmD, Safety Evaluator  
Division of Medication Error Prevention and Analysis

Subject: Proprietary Name Review

Drug Name: Oleptro (Trazodone HCl) Extended-release Tablets  
150 mg and 300 mg

Application Type/Number: NDA 22-411 (IND 76,137)

Applicant: Labopharm

OSE RCM #: 2008-1551

**\*\*This document contains proprietary and confidential information that should not be released to the public.\*\***

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## EXECUTIVE SUMMARY

The results of the Proprietary Name Risk Assessment found that the proposed name, Oleptro, is not vulnerable to name confusion that could lead to medication errors. Thus, DMEPA has no objections to the use of the proprietary name, Oleptro for this product.

However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, DMEPA rescinds this Risk Assessment finding, and recommends that the name be resubmitted for review. Additionally, if the product approval is delayed beyond 90 days from the signature date of this review, the proposed name must be resubmitted for evaluation.

## 1 BACKGROUND

### 1.1 INTRODUCTION

This review was written in response to a request from the Division of Psychiatry Products for an assessment of the proprietary name, “Oleptro”, regarding potential name confusion with other proprietary and established drug names. The Applicant submitted an independent name risk assessment conducted by (b) (4) for the name Oleptro, and the assessment was evaluated as part of this review.

Container/Blister labels, blister carton and insert labeling were also provided to be evaluated from a medication errors perspective. Review comments will be provided under a separate cover in a forthcoming review managed under the same review number (OSE 2008-1551).

### 1.2 PRODUCT INFORMATION

Oleptro is the proposed name for Trazodone HCl Extended-release caplets. Trazodone HCl is a serotonin 2A antagonist reuptake inhibitor and is indicated for the treatment of major depressive disorder.

The recommended starting dosage is 150 mg per day. The usual dose is 300 mg per day and the maximum daily dose should not exceed 375 mg. Oleptro should be taken orally at the same time every day in the late evening.

Oleptro will be available as 150 mg and 300 mg bisectable tablets.

## 2 METHODS AND MATERIALS

This section describes the methods and materials used by the DMEPA staff conducting a proprietary name risk assessment (see 2.1 Proprietary Name Risk Assessment). The primary focus of the assessment is to identify and remedy potential sources of medication error prior to drug approval. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.<sup>1</sup>

### 2.1 PROPRIETARY NAME RISK ASSESSMENT

FDA’s Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name, Oleptro, and the proprietary and established names of drug products

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<sup>1</sup> National Coordinating Council for Medication Error Reporting and Prevention.  
<http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.

existing in the marketplace and those pending IND, BLA, NDA, and ANDA products currently under review by CDER.

For the proprietary name, Oleptro, the DMEPA staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity (see Sections 2.1.1 for detail) and held an CDER Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see 2.1.1.2).

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name (see detail 2.1.4). The overall risk assessment is based on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and is focused on the avoidance of medication errors. FMEA is a systematic tool for evaluating a process and identifying where and how it might fail.<sup>2</sup> FMEA is used to analyze whether the drug names identified with look- or sound-alike similarity to the proposed name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of the medication error staff to anticipate the conditions of the clinical setting that the product is likely to be used in based on the characteristics of the proposed product.

In addition, the product characteristics provide the context for the verbal and written communication of the drug names and can interact with the orthographic and phonetic attributes of the names to increase the risk of confusion when there is overlap, or, in some instances, decrease the risk of confusion by helping to differentiate the products through dissimilarity. As such, the staff considers the product characteristics associated with the proposed drug throughout the risk assessment, since the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed drug name include, but are not limited to established name of the proposed product, the proposed indication, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, DMEPA considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.<sup>3</sup>

### **2.1.1 Search Criteria**

The DMEPA staff considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted as outlined in Appendix A.

For this review, particular consideration was given to drug names beginning with the letter ‘O’ when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.<sup>45</sup>

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<sup>2</sup> Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

<sup>3</sup> Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

<sup>4</sup> Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at <http://www.ismp.org/Tools/confuseddrugnames.pdf>

To identify drug names that may look similar to Oleptro, the staff also consider the other orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (seven letters), upstrokes (three, capital letter ‘O’, ‘I’, and ‘t’), downstrokes (one, if “p” is scripted), cross-strokes (one, ‘t’), and dotted letters (none). Additionally, several letters in Oleptro may be vulnerable to ambiguity when scripted, including the letter ‘O’ may appear as ‘A’ or ‘U’; lower case ‘o’ appear as a lower case ‘a’ or ‘u’. As such, the staff should also consider these alternate appearances when identifying drug names that may look similar to Oleptro.

When searching to identify potential names that may sound similar to Oleptro, the medication error staff search for names with similar number of syllables (three), stresses (O- lep-tro or o-LEP-tro or o-lep-TRO), consonant sound pronunciation (“O versus “UH” or ‘-lep-’ versus ‘-leap-’), and placement of vowel and consonant sounds. In addition, several letters in Oleptro may be subject to misinterpretation when spoken, including the letter ‘O’ which may be interpreted as ‘U’ and the letter ‘e’ may be misinterpreted as ‘i’. As such, the staff also considers these alternate pronunciations when identifying drug names that may sound similar to Oleptro. The Applicant’s intended pronunciation of the proprietary name could not be expressly taken into consideration, as this was not provided with the proposed name submission.

The staff also consider the product characteristics associated with the proposed drug throughout the identification of similar drug names, since the product characteristics of the proposed drug ultimately determine the use of the product in the clinical practice setting. For this review, the DMEPA staff were provided with the following information about the proposed product: the proposed proprietary name (Oleptro), the established name (Trazadone HCl), proposed indication (treatment of major depressive disorder (MDD)), strength (150 mg and 300 mg), dose (150 mg to 375 mg per day), frequency of administration (once daily), route (oral) and dosage form of the product (tablet). Appendix A provides a more detailed listing of the product characteristics the medication error staff generally takes into consideration.

Lastly, the DMEPA staff also considers the potential for the proposed name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. As such, these broader safety implications of the name are considered and evaluated throughout this assessment and the medication error staff provides additional comments related to the safety of the proposed name or product based on their professional experience with medication errors.

#### **2.1.1.1 Databases and Information Sources**

The proposed proprietary name, Oleptro, was provided to the medication error staff of DMEPA to conduct a search of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to Oleptro using the criteria outlined in 2.1.1. A standard description of the databases used in the searches is provided in Section 6. To complement the process, the medication error staff uses a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the medication error staff reviews the USAN stem list to determine if any USAN stems are present within the proprietary name. The findings of the individual Safety Evaluators are then pooled and presented to the Expert Panel.

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<sup>5</sup> Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artificial Intelligence in Medicine (2005)



### 2.1.1.2 CDER Expert Panel Discussion

An Expert Panel Discussion is held by DMEPA to gather CDER professional opinions on the safety of the product and the proprietary name, Oleptro. Potential concerns regarding drug marketing and promotion related to the proposed names are also discussed. This group is composed of the DMEPA Staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC).

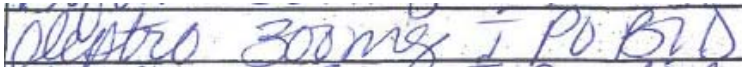
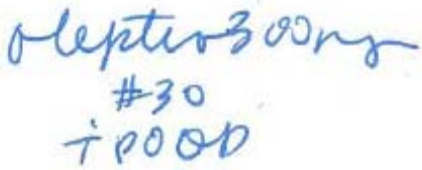
The pooled results of the medication error staff were presented to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend the addition of names, additional searches by the Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

### 2.1.2 FDA Prescription Analysis Studies

Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Oleptro with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. The studies employ a total of 122 healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The results are used by the Safety Evaluator to identify any orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of Oleptro in handwriting and verbal communication of the name, inpatient medication orders and outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These prescriptions are optically scanned and one prescription is delivered to a random sample of 122 participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants send their interpretations of the orders via e-mail to the medication error staff.

**Figure 1. Oleptro Study (conducted on November 20, 2008)**

HANDWRITTEN PRESCRIPTION AND MEDICATION ORDER	VERBAL PRESCRIPTION
<u>Inpatient Prescription Order:</u> 	Oleptro # 30 1 tablet po daily.
<u>Outpatient Medication Order :</u> 	

### **2.1.3 External Proprietary Name Risk Assessment**

For this product, the applicant submitted an independent risk assessment of the proposed proprietary name conducted by a consulting firm. The DMEPA staff conducts an independent analysis and evaluation of the data provided, and responds to the overall findings of the assessment. When the external proprietary name risk assessment identifies potentially confusing names that were not captured in the staff's database searches or in the Expert Panel Discussion, these names are included in the Safety Evaluator's Risk Assessment and analyzed independently by the Safety Evaluator to determine if the potentially confusing name could lead to medication errors in usual practice settings.

After the Safety Evaluator has determined the overall risk assessment of the proposed name, the Safety Evaluator compares the findings of their overall risk assessment with the findings of the proprietary name risk assessment submitted by the Applicant. The Safety Evaluator then determines whether the DMEPA staff's risk assessment concurs or differs with the findings. When the proprietary name risk assessments differ, we provide a detailed explanation of these differences.

### **2.1.4 Safety Evaluator Risk Assessment of the Proposed Proprietary Name**

Based on the criteria set forth in Section 2.1.1, the Safety Evaluator Risk Assessment applies their individual expertise gained from evaluating medication errors reported to FDA to conduct a Failure Mode and Effects Analysis and provide an overall risk of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.<sup>6</sup> When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed name to be confused with another drug name as a result of the name confusion and cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to look- or sound-alike drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is not yet marketed, the Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Appendix A. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure mode and the effects associated with the failure mode.

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name to all of the names gathered from the above searches, expert panel evaluation, and studies, and identifies potential failure mode by asking: "Is the name Oleptro convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting?" An affirmative answer indicates a failure mode and represents a potential for Oleptro to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names possess similarity that would cause confusion at any point in the medication use system and the name is eliminated from further review.

In the second stage of the Risk Assessment, all potential failure modes are evaluated to determine the likely *effect* of the drug name confusion, by asking "Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?" The answer to this question is a central component of the Safety Evaluator's overall risk assessment of the proprietary name.

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<sup>6</sup> Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

If the Safety Evaluator determines through FMEA that the name similarity would ultimately not be a source of medication errors in the usual practice setting, the name is eliminated from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend that an alternate proprietary name be used. In rare instances, the FMEA findings may provide other risk-reduction strategies, such as product reformulation to avoid an overlap in strength or an alternate modifier designation may be recommended as a means of reducing the risk of medication errors resulting from drug name confusion.

DMEPA will object to the use of proposed proprietary name when the one or more of the following conditions are identified in the Safety Evaluator's Risk Assessment:

1. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the review Division concurs with DDMAC's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a trade name or otherwise. [21 U.S.C 321(n); see also 21 U.S.C. 352(a) & (n)].
2. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].
3. FMEA identifies potential for confusion between the proposed proprietary name and other proprietary or established drug names, and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
4. The proposed proprietary name contains an USAN stem, particularly in a manner that is contradictory to the USAN Council's definition.
5. DMEPA staff identifies a potential source of medication error within the proposed proprietary name. The proprietary name may be misleading, or inadvertently introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

In the event that DMEPA objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, DMEPA will provide a contingency objection based on the date of approval: whichever product is awarded approval first has the right to the use the name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

If none of these conditions are met, then DMEPA will not object to the use of the proprietary name. If any of these conditions are met, then DMEPA will object to the use of the proprietary name. The threshold set for objection to the proposed proprietary name may seem low to the Applicant; however, the safety concerns set forth in criteria 1 through 5 are supported either by FDA Regulation or by external healthcare authorities, including the IOM, WHO, JCAHO, and ISMP, have examined medication errors resulting from look- or sound-alike drug names and called for Regulatory Authorities to address the issue prior to approval.

Furthermore, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and preventable source of medication error that, in many instances, can be identified and remedied prior to approval to avoid patient harm.

Additionally, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to remedy post-approval. Educational efforts and so on are low-leverage strategies that have proven to have limited effectiveness at alleviating the

medication errors involving drug name confusion. Higher-leverage strategies, such as drug name changes, have been undertaken in the past; but at great financial cost to the Applicant, and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for the approving the error-prone proprietary name. Moreover, even after Applicant's have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioner's vocabulary, and as such, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval (see limitations of the process).

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the FMEA process is used to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the Applicant select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name, and so DMEPA may be able to provide the Applicant with recommendations that reduce or eliminate the potential for error would render the proposed name acceptable.

### **3 RESULTS**

#### **3.1 PROPRIETARY NAME RISK ASSESSMENT**

##### ***3.1.1 Databases and Information Sources***

The search of the internet and several standard published databases and information sources (see Section 6 References) identified a total of 13 names as having some similarity to the name Oleptro.

Nine of the 13 names were thought to look like Oleptro, which include: Astepro, Olestra, Aleptolan, (b) (4), Allergra, Alophen, Olopatadine, Olester, and Avapro. Two names (Septra and Kaletra) were thought to sound like Oleptro. Two names, Optro and Elestrin, were thought to look and sound similar to Oleptro.

A search of the United States Adopted Name (USAN) stem list on November 21, 2008 identified no USAN stems within the proposed name, Oleptro. As such, a total of 13 names were analyzed to determine if the drug names could be confused with Oleptro and if the drug name confusion would likely result in a medication error.

##### ***3.1.2 CDER Expert Panel Discussion***

The Expert Panel reviewed the pool of names identified by the DMEPA staff (see section 3.1.1. above), and recommended that independent searches consider the potential for confusion with drug names beginning with the letter 'H'.

DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name.

##### ***3.1.3 FDA Prescription Analysis Studies***

A total of 32 practitioners responded. None of the responses overlap with any existing or proposed drug names. About forty-seven percent of the participants (n=15) interpreted the name correctly as "Oleptro". The misinterpretations occurred in the voice prescription study, the inpatient and outpatient written prescription studies with the prefix reported as 'Ale-', 'Oles-', 'Desuffixes in Oleptro reported as '-tio', '-tra', '-tiv', and '-teo' instead of '-tro' and the suffix

reported as ‘-tac’ or ‘-tak’ instead of ‘-taq’. In the written prescription studies, the suffix was misinterpreted as ‘-tag’. See Appendix B for the complete listing of interpretations from the verbal and written prescription studies.

### **3.1.4 External Proprietary Name Risk Assessment**

In the (b) (4) Tradename Survey and Evaluation submitted by the Applicant, (b) (4) identified and evaluated a total of 14 drug names thought to have some potential for confusion with the name (b) (4).

Eleven of the 14 names (Carbatrol, Clozapine, Colestid, Equetro, Lexapro, Lipitor, Olanzapine, Orlistat, Oxistat, Prempro, and Trileptal), were not previously identified in the medication error staff searches or the Expert Panel Discussion. (b) (4) did not believe any of the identified drugs names represented a significant risk of confusion due to “differences in name construction”.

Seven of the 14 names (Allegra, Carbatrol, Equetro, Olanzapine, Orlistat, Oxistat, and Trileptal) were thought by practitioners to look and sound similar to Oleptro. The remaining 7 names (Avapro, Clozapine, Colestid, Lexapro, Lipitor, Prempro, and Septra) were thought to look like Oleptro. Each of the names were examined in detail, taking into account the number of syllables, overlapping letter strings, and letter structure (ascending and descending letters when scripted).

A review of the (b) (4) data noted that the name Allegra identified by the DMEPA staff as having look-alike similarity to Oleptro was thought by the practitioners consulted in the (b) (4) study to also have some sound-alike similarity. Similarly, the (b) (4) data noted that the name Septra looked like Oleptro, whereas our staff identified the name as having sound-alike similarity.

### **3.1.5 Safety Evaluator Risk Assessment of the Proposed Proprietary Name**

Independent searches by the primary Safety Evaluator identified two additional names (Alimta and Alista) thought to look similar to Oleptro and represent a potential source of drug name confusion. As such, a total of 26 names were analyzed to determine if the drug names could be confused with Oleptro and if the drug name confusion would likely result in a medication error.

Fourteen of the 26 names (i.e. Carbatrol, Clozapine, Colestid, Elestrin, Equetro, Kaletra, Lexapro, Lipitor, Olanzapine, Opatadine, Orlistat, Oxistat, Prempro, and Trileptal) lacked orthographic and/or phonetic similarity (Appendix C). Two names were not evaluated further because confusion with these names was determined to be unlikely. The name, Olester, is a chemical substance identified in Micromedex, specifically in the List of Lists (LOLI) database but was not identified as an active ingredient in any drug product. Similarly, the name, Olestra, is a fat substitute that has been used in the preparation of traditionally high-fat foods and is not available as a drug product.

The remaining 10 names were determined to have some orthographic and/or phonetic similarity to Oleptro, and thus determined to present some risk for confusion. Failure mode and effects analysis was then applied to determine if the proposed name, Oleptro, could potentially be confused with any of the 10 names and lead to medication error.

The FMEA determined that the name similarity between Oleptro and the identified names was unlikely to result in medication errors for all 10 products for reasons described/outlined in Appendices E through H.

Furthermore, we note that the Applicant uses the terms “bisectable” and “caplet” to describe the dosage form. However, these terms are not recognized by the CDER Data Standards manual.

## 4 DISCUSSION

### 4.1 PROPRIETARY NAME RISK ASSESSMENT

We analyzed 10 names for their similarity to the proposed name Oleptro. The findings of the FMEA indicate that the proposed name does not appear to be vulnerable to name confusion that could lead to medication errors with any of the names evaluated.

However, we note the use of the terms, “bisectable” and “caplet” which are not listed in the CDER Data Standards manual. We suggest consulting with Chemistry, Manufacturing, and Control (CMC) regarding the use of the terms “bisectable” and “caplet” to evaluate the appropriateness of the terms.

## 5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Oleptro, is not vulnerable to name confusion that could lead to medication errors. As such, DMEPA does not object to the use of the proprietary name, Oleptro, for this product at this time. However, if any of the proposed product characteristics as stated in this review are altered prior to submission of the NDA or approval of the product, DMEPA rescinds this Risk Assessment finding. If the product approval is delayed beyond 90 days from the date of this review, the proposed name must be resubmitted for evaluation. If the product approval is delayed beyond 90 days from the date of this review, the proposed name must be resubmitted for evaluation.

### 5.1 COMMENTS TO THE DIVISION

Please consult with CMC to evaluate the appropriateness of the terms “bisectable” and “caplet”, used to describe the dosage form.

DMEPA would appreciate feedback on the final outcome of this review. We would be willing to meet with the Division for further discussion, if needed. Please copy DMEPA on any correspondence to the Applicant pertaining to this issue. If you have further questions or need clarifications, please contact Abolade Adeolu, OSE Project Manager, at 301-796-4264.

### 5.2 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Oleptro, and have concluded that it is acceptable.

The proposed proprietary name, Oleptro, will be re-reviewed 90 days prior to the approval of the NDA. If we find the name unacceptable following the re-review, we will notify you.

If any of the proposed product characteristics are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

## 6 REFERENCES

### 1. *Micromedex Integrated Index* (<http://csi.micromedex.com>)

Contains a variety of databases covering pharmacology, therapeutics, toxicology and diagnostics.

### 2. *Phonetic and Orthographic Computer Analysis (POCA)*

As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists which operates in a similar fashion. This is a database which was created for the Division of Medication Error Prevention and Analysis, FDA.

3. ***Drug Facts and Comparisons, online version, St. Louis, MO***  
 (<http://factsandcomparisons.com>)

Drug Facts and Comparisons is a compendium organized by therapeutic course; contains monographs on prescription and OTC drugs, with charts comparing similar products.

4. ***AMF Decision Support System [DSS]***

DSS is a government database used to track individual submissions and assignments in review divisions.

5. ***Division of Medication Errors Prevention and Analysis proprietary name consultation requests***

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis from the Access database/tracking system.

6. ***Drugs@FDA*** (<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>)

Drugs@FDA contains most of the drug products approved since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA approved [brand name](#), [generic drugs](#), [therapeutic biological products](#), [prescription](#) and [over-the-counter](#) human drugs and [discontinued drugs](#) and “[Chemical Type 6](#)” approvals.

7. ***Electronic online version of the FDA Orange Book***  
 (<http://www.fda.gov/cder/ob/default.htm>)

Provides a compilation of approved drug products with therapeutic equivalence evaluations.

8. ***U.S. Patent and Trademark Office*** (<http://www.uspto.gov>)

Provides information regarding patent and trademarks.

9. ***Clinical Pharmacology Online*** ([www.clinicalpharmacology-ip.com](http://www.clinicalpharmacology-ip.com))

Contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. Provides a keyword search engine.

10. ***Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at***  
 ([www.thomson-thomson.com](http://www.thomson-thomson.com))

The Pharma In-Use Search database contains over 400,000 unique pharmaceutical trademarks and trade names that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

11. ***Natural Medicines Comprehensive Databases*** ([www.naturaldatabase.com](http://www.naturaldatabase.com))

Contains up-to-date clinical data on the natural medicines, herbal medicines, and dietary supplements used in the western world.

12. ***Stat!Ref*** ([www.statref.com](http://www.statref.com))

Contains full-text information from approximately 30 texts. Includes tables and references. Among the database titles are: Handbook of Adverse Drug Interactions, Rudolphs Pediatrics, Basic Clinical Pharmacology and Dictionary of Medical Acronyms Abbreviations.

**13.     *USAN Stems*** (<http://www.ama-assn.org/ama/pub/category/4782.html>)

List contains all the recognized USAN stems.

**14.     *Red Book Pharmacy's Fundamental Reference***

Contains prices and product information for prescription, over-the-counter drugs, medical devices, and accessories.

**15.     *Lexi-Comp*** ([www.lexi.com](http://www.lexi.com))

A web-based searchable version of the Drug Information Handbook.

**16.     *Medical Abbreviations Book***

Contains commonly used medical abbreviations and their definitions.



## APPENDICES

### Appendix A:

The medication error staff considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compare the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. The medication error staff also examines the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly *and* dissimilarly spelled drug name pairs to appear very similar to one another and the similar appearance of drug names when scripted has lead to medication errors. The medication error staff apply their expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (i.e. “T” may look like “F,” lower case ‘a’ looks like a lower case ‘u,’ etc), along with other orthographic attributes that determine the overall appearance of the drug name when scripted (see detail in Table 1 below). Additionally, since verbal communication of medication names is common in clinical settings, the medication error staff compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names. If provided, DMEPA will consider the Applicant’s intended pronunciation of the proprietary name. However, because the Applicant has little control over how the name will be spoken in practice, DMEPA also considers a variety of pronunciations that could occur in the English language.

**Table 1.** Criteria used to identify drug names that look- or sound-similar to a proposed proprietary name

Type of similarity	Considerations when searching the databases		
	Potential causes of drug name similarity	Attributes examined to identify similar drug names	Potential Effects
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	<ul style="list-style-type: none"> <li>Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication</li> <li>Names may look similar when scripted and lead to drug name confusion in written communication</li> </ul>
	Orthographic similarity	Similar spelling Length of the name Upstrokes Downstrokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters	<ul style="list-style-type: none"> <li>Names may look similar when scripted, and lead to drug name confusion in written communication</li> </ul>

		Overlapping product characteristics	
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	<ul style="list-style-type: none"> <li>Names may sound similar when pronounced and lead to drug name confusion in verbal communication</li> </ul>

### **Appendix B:** FDA Prescription Study Responses

	Voice Prescription	Outpatient Medication Order
Oleptro	Oleptro	Oleptio
Oleptro	Oleptro	Oleptro
Aleptro	Aleptro	Oleptiv
Oleptro	Aleptro	Oleptio
Aleptro		Olepteo
Oleptro		Oleptio
Oleptro		Oleptiv
Oleptro		Oleptio
Oleptro		Olepteo
Oleptro		Oleptio
Oleptro		
Oleptro		
Oleptro		
Deptro		
Oleptro		
Aleptro		
Oleptro		
Oleptro		

**Appendix C:** Names that lack convincing orthographic and/or phonetic similarities

Name	Similarity to Oleptro
Carbatrol	Look and Sound
Clozapine	Look
Colestid	Look
Elestrin	Look and Sound
Equetro	Look and Sound
Kaletra	Sound
Lexapro	Look
Lipitor	Look
Olanzapine	Look and Sound
Olopatadine	Look
Orlistat	Look and Sound
Oxistat	Look and Sound
Prempro	Look
Trileptal	Look and Sound

**Appendix D:** Products which are not drugs

Name	Similarity to Oleptro	
Olestra	Look	This is a fat substitute used in the preparation of traditionally high-fat foods.
Olester	Look	This is a chemical substance identified in Micromedex, specifically in the List of Lists (LOLI) database but was not identified as an active ingredient in any drug product.

**Appendix E:** Proprietary names used only in Foreign Countries

Proprietary Name	Similarity to Oleptro	Country
Aleptolan	Look	Estonia, Lithuania, Latvia – active ingredient is risperidone.
Alista	Look	Indonesia – active ingredient is a cilostazol.

**Appendix F:** Product whose proposed proprietary names is still in Phase II studies.

Name	Similarity to Oleptro	Status
Optro <sup>***</sup>	Look and Sound	Per online Facts and Comparisons database, the drug product is in Phase IIa studies and not an approved product.

**Appendix G:** Products with no numerical overlap in strength and dose.

Product name with potential for confusion	Similarity to Oleptro	Strength	Usual Dose
Oleptro (Trazodone HCl)		150 mg, 300 mg	Usual dose: 150 mg to 300 mg daily.
(b) (4)	Look	(b) (4)	(b) (4)
Septa (Sulfamethoxazole/Trimethoprim)	Look	400 mg/80 mg	<i>Acute infective exacerbation of COPD:</i> 2 tablets every 12 hours for 14 days. <i>Pneumocystis pneumonia:</i> 320 mg TMP component/day three times daily for 21 days <i>Pneumocystis pneumonia prophylaxis:</i> 1 tablet daily or 2 tabs 3 times a week. <i>Shigellosis:</i> 1 tablet every 12 hours

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			<p>for 5 days.</p> <p><i>Toxoplasma encephalitis prophylaxis:</i> 1 tablet daily.</p> <p><i>Traveler's diarrhea:</i> 2 tablets every 12 hours for 5 days</p> <p><i>Urinary Tract Infection:</i> 2 tablets every 12 hours for 10-14 days.</p>
Alimta (Pemetrexed)	Look	100 mg, 500 mg	<p><i>Malignant pleural mesothelioma and non-small cell lung cancer:</i> combination use with cisplatin – 500 mg/m<sup>2</sup> as an infusion over 10 minutes on day 1 of each 21-day cycle.</p> <p><i>Non-small cell lung cancer (w/o cisplatin):</i> 500 mg/m<sup>2</sup> administered intravenously over 10 minutes on day 1 of each 21-day cycle.</p>

**Appendix H:** Potential confusing name with numerical overlap in dose or achievable dose.

Oleptro (Trazodone HCl)	150 mg, 300 mg	Usual dose: 150 mg to 300 mg daily.
Failure Mode: Name confusion	Causes (could be multiple)	Effects
Astepro <sup>***</sup> (Azelastine HCl)	<p>Orthographic similarity – Both names begin with letters that resemble each other when scripted (“A” versus “O” and end with similar suffixes (“-pro” versus “-ptro”). Additionally, both names are seven letters long.</p> <p>Both products have a numerical similarity in strengths [30 mL (1 mg/mL) versus 300 mg].</p>	<p>Orthographic and product differences in the drug products minimize the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i></p> <p>When written, the names appear similar, however, the placement of the upstroke, cross-stroke, and/or downstroke letters in Astepro and Oleptro, help to distinguish the two names from each other. Additionally, while there is a numerical overlap in strengths, the dosage form, route of administration, and frequency of administration vary. Thus, despite some overlapping product characteristics, we believe the risk of medication error is minimized by the placement of the upstroke, downstroke, and cross-stroke letters, as well as the differences in their product characteristics.</p>

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<p>Allegra (Fexofenadine HCl)</p>	<p>Orthographic similarity - Both names begin with similar looking prefixes (“All-” versus “Ole-”) and end with letters that can also resemble each other (“a” versus “o”). Both names are also seven letters long.</p> <p>Both have overlapping routes of administration (oral), dosage form (tablet), frequency of administration (once daily), and a numerical similarity (30 mg versus 300).</p>	<p>Orthographic differences in the names minimize the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i></p> <p>When written the names appear similar, however, the presence of a cross-stroke letter, ‘t’ in Oleptro, and the positioning of the downstroke letters, ‘g’ and ‘p’, in Allegra and Oleptro, respectively, helps to distinguish Allegra from the proposed name, Oleptro. While the strengths, route of administration overlap, frequency of administration, and dosage form overlap, it is difficult to ignore the differences in their orthographic appearance. Thus, despite some overlapping product characteristics, we believe the risk for medication error is minimized by the presence of the cross-stroke letter in Oleptro, and placement of the downstroke letters in Allegra and Oleptro, in addition to the differences in their product characteristics.</p>
<p>Alophen (Bisacodyl) – Over-the-Counter</p>	<p>Orthographic similarity - Both names begin with similar looking prefixes (“Alo-” versus “Ole-”) and have infixes that resemble each other when scripted (“-op-” versus “-ep-”). Both names are also seven letters long.</p> <p>Both have overlapping routes of administration (oral), dosage form (tablet), and frequency of administration (once daily).</p>	<p>Orthographic differences in the names minimize the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i></p> <p>When written the names appear similar, however, the presence of a cross-stroke letter, ‘t’ in Oleptro, helps to distinguish Alophen from the proposed name, Oleptro. While the strengths do not overlap, the dose of 15 mg, which is an achievable dose for Alophen, numerically overlaps with 150 mg, a dosage for Oleptro. In addition, both products are available as tablets/caplets and are administered once daily. Nonetheless, we believe the risk for medication error is minimized by the presence of the cross-stroke letter in Oleptro and the availability of Alophen as an over-the-counter product as opposed to Oleptro which is available by prescription only.</p>

Avapro (Irbesartan)	<p>Orthographic similarity – Both names begin with similar looking letters “A” versus “O” and end with similar suffixes (“-pro” versus “-ptro”). Additionally, both names are similar in length (six letters versus seven).</p> <p>Both have overlapping routes of administration, dosage form (tablet), frequency of administration (once daily), and strengths (150 mg and 300 mg).</p>	<p>Orthographic differences in the names minimize the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i></p> <p>When written the names appear similar, however, the presence of the upstroke letter “l” and cross-stroke letter “t” in Oleptro, helps to differentiate this name from Avapro, which has a downstroke letter “p” in Avapro. While the product characteristics overlap, the differences in their orthographic characteristics help to minimize the risk for medication error.</p>
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